Generation and Cycloaddition Behavior of Spirocyclic Carbonyl Ylides. Application to the Synthesis of the Pterosin Family of Sesquiterpenes†

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The Rh(II)-catalyzed reaction of 1-acetyl-1-(diazoacetyl)cyclopropane and ethyl 3-(1-acetyl-cyclopropyl)-2-diazo-3-oxopropiolate with various dipolarophiles afforded dipolar cycloadducts in good yield. The reaction involves the formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the adjacent keto group to generate a five-membered cyclic carbonyl ylide which undergoes a subsequent dipolar cycloaddition reaction. The regiochemical results encountered can be rationalized on the basis of FMO considerations. For carbonyl ylides, the HOMO dipole is dominant for reactions with electron deficient dipolarophiles, while the LUMO becomes important for cycloaddition to more electron rich species. A short synthesis of several members of the pterosin family of sesquiterpenes is described in which the key step involves a dipolar cycloaddition using a carbonyl ylide. The Rh(II)-catalyzed reaction of 1-acetyl-1-(diazoacetyl)-cyclopropane with cyclopentenone afforded a dipolar cycloadduct in good yield as a 4:1 mixture of diastereomers. Treatment of the major cycloadduct with triphenylphosphonium bromide in the presence of sodium hydride gave the expected Wittig product. The reaction of this compound with acid in the presence of various solvents gave rise to several members of the pterosin family. The overall sequence of reactions can best be described as proceeding by an initial oxy-bridge ring opening followed by dehydration and a subsequent acid-catalyzed cyclopropyl ring opening. The facility of the process is undoubtedly related to the aromaticity gained in the final step.

Tandem reactions provide an opportunity for linking the synthetic power of two or more transformations in a single operation.[1−6] These reactions are among the most powerful building tools available since they rapidly increase the complexity of a substrate starting from relatively simple precursors. Important contributions to this area have been realized utilizing a combination of cationic,[7,8] anionic,[9] radical,[10] pericyclic,[11] and transition metal catalyzed processes.[12] In recent years, the tandem cyclization−cycloaddition chemistry of rhodium carbenoids has been developed in these laboratories as a general approach to oxabicyclic ring systems.[13] The overall sequence involves the generation of the rhodium carbenoid from an α-diazo keto precursor followed by a

† This paper is dedicated to Professor Michael P. Cava on the occasion of his 70th birthday.

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(1) Ho, T. L. *Tandem Organic Reactions;* Wiley-Interscience: New York, 1992.

(2) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32,* 31.

(3) Ziegler, F. E. In *Comprehensive Organic Synthesis, Combining C-C π-Bonds*; Paquette, L. A., Ed.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 7.3.

(4) Curran, D. P. *Synlett* **1991**, 63.

(5) (a) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1983**, *56,* 2073. (b) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Chem. Lett.* **1983**, 519. (c) Kanemasa, S.; Takenaka, S.; Watanabe, H.; Tsuge, O. *J. Org. Chem.* **1989**, *54,* 420.

(6) Roxburgh, C. J. *Tetrahedron* **1993**, *49,* 10749.

(7) Sutherland, J. K. In *Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 341.

(8) (a) Bartlett, P. A. In *Asymmetric Synthesis;* Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3. (b) Fish, P. V.; Johnson, W. S. *J. Org. Chem.* **1994**, *59,* 2324. (c) Jacobsen, E. J.; Levin, J.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110,* 4329. (d) Johnson, W. S.; Fletcher, V. R.; Chenera, B.; Bartlett, W. R.; Tham, F. S.; Kullnig, R. K. *J. Am. Chem. Soc.* **1993**, *115,* 497. (e) Guay, D.; Johnson, W. S.; Schubert, U. *J. Org. Chem.* **1989**, *54,* 4731.

(9) (a) Canonne, P.; Boulanger, R.; Bernatchez, M. *Tetrahedron Lett.* **1987**, *28,* 4997. (b) Bailey, W. F.; Ovaska, T. V. *Tetrahedron Lett.* **1990**, *31,* 627. (c) Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110,* 4788. (d) Utimoto, K.; Imi, K.; Shiragami, H.; Fujikura, S.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26,* 2101. (e) Fujikura, S.; Inoue, M.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25,* 1999. (f) Oppolzer, W.; Pitteloud, R.; Strauss, H. F. *J. Am. Chem. Soc.* **1982**, *104,* 6476. (g) Bunce, R. A.; Dowdy, E. D.; Jones, P. B.; Holt, E. M. *J. Org. Chem.* **1993**, *58,* 7143 and references therein. (h) Bunce, R. A.; Harris, C. R. *J. Org. Chem.* **1992**, *57,* 6981.

(10) (a) Motherwell, W. B.; Crich, D. *Free Radical Reactions in Organic Synthesis;* Academic Press: London, 1991. (b) Curran, D. P. In *Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, Chapter 4.2. (c) Mowbray, C. E.; Pattenden, G. *Tetrahedron Lett.* **1993**, *34,* 127 and references therein. (d) Hitchcock, S. A.; Pattenden, G. *Tetrahedron Lett.* **1992**, *33,* 4843. (e) Curran, D. P.; Sisko, J.; Yeske, P. E.; Liu, H. *Pure Appl. Chem.* **1993**, *65,* 1153. (f) Curran, D. P.; Shen, W. *Tetrahedron* **1993**, *49,* 755. (g) Parker, K. A.; Fokas, D. *J. Am. Chem. Soc.* **1992**, *114,* 9688. (h) Chen, Y.-J.; Chen, C.-M.; Lin, W.-Y. *Tetrahedron Lett.* **1993**, *34,* 2961. (i) Batey, R. A.; Harling, J. D.; Motherwell, W. B. *Tetrahedron* **1992**, *48,* 8031. (j) Ozlu, Y.; Cladingboel, D. E.; Parsons, P. J. *Synlett* **1993**, 357. (k) Grissom, J. W.; Klingberg, D. *J. Org. Chem.* **1993**, *58,* 6559 and references therein.

(11) (a) Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1994**, *59,* 4576. (b) Denmark, S. E.; Stolle, A.; Dixon, J. A.; Guagnano, V. *J. Am. Chem. Soc.* **1995**, *117,* 2100. (c) Markó, I. E.; Seres, P.; Swarbrick, T. M.; Staton, I.; Adams, H. *Tetrahedron Lett.* **1992**, *33,* 5649 and references therein. (d) Guevel, R.; Paquette, L. A. *J. Am. Chem. Soc.* **1994**, *116,* 1776 and references therein. (e) Jisheng, L.; Gallardo, T.; White, J. B. *J. Org. Chem.* **1990**, *55,* 5426. (f) Sunitha, K.; Balasubramanian, K. K.; Rajagopalan, K. *Tetrahedron Lett.* **1985**, *26,* 4393. (g) Wender, P. A.; Sieburth, S. M.; Petraitis, J. J.; Singh, S. K. *Tetrahedron* **1981**, *37,* 3976 and references therein.

(12) (a) Snider, B. B.; Vo, N. H.; Foxman, B. M. *J. Org. Chem.* **1993**, *58,* 7228 and references therein. (b) Iwasawa, N.; Funahashi, M.; Hayakawa, S.; Narasaka, K. *Chem. Lett.* **1993**, 545. (c) Ali, A.; Harrowven, D. C.; Pattenden, G. *Tetrahedron Lett.* **1992**, *33,* 2851. (d) Grigg, R.; Kennewell, P.; Teasdale, A. J. *Tetrahedron Lett.* **1992**, *33,* 7789 and references therein. (e) Batty, D.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3205 and references therein. (f) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1992**, *114,* 791. (g) Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56,* 3817. (h) Kim, O. K.; Wulff, W. D.; Jiang, W.; Ball, R. G. *J. Org. Chem.* **1993**, *58,* 5571.

(13) (a) Padwa, A.; Carter, S. P.; Nimmesgern, H.; Stull, P. *J. Am. Chem. Soc.* **1988**, *110,* 2894. (b) Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Org. Chem.* **1988**, *53,* 2875. (c) Padwa, A.; Chinn, R. L.; Hornbuckle, S. F.; Zhi, L. *Tetrahedron Lett.* **1989**, *30,* 301. (d) Padwa, A.; Chinn, R. C.; Zhi, L. *Tetrahedron Lett.* **1989**, *30,* 1491. (e) Padwa, A.; Hertzog, D. L.; Chinn, R. C. *Tetrahedron Lett.* **1989**, *30,* 4077. (f) Padwa, A.; Dean, D. C.; Zhi, L. *J. Am. Chem. Soc.* **1989**, *111,* 6451. (g) Padwa, A.; Dean, D. C.; Krumpe, K. E. *J. Chem. Soc., Chem. Commun.* **1989**, 921. (h) Hertzog, D. L.; Nadler, W. R.; Zhang, Z. J.; Padwa, A. *Tetrahedron Lett.* **1992**, *33,* 5877.

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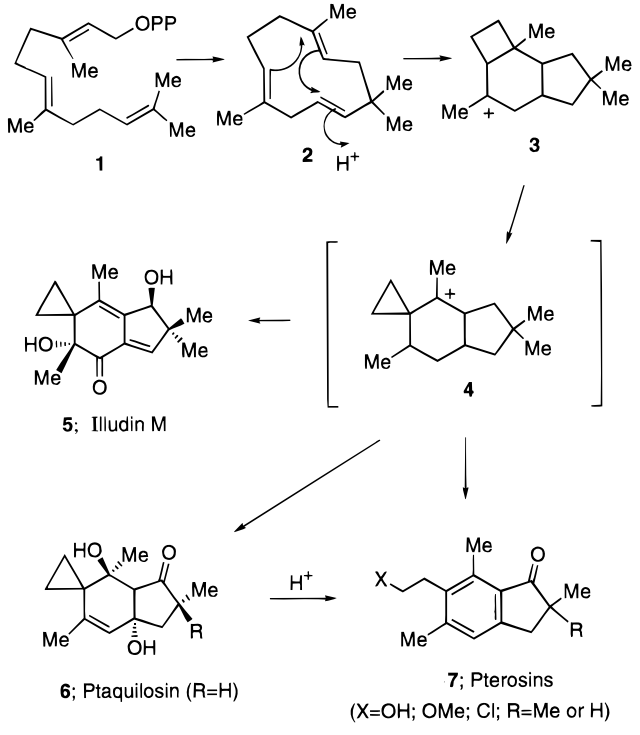
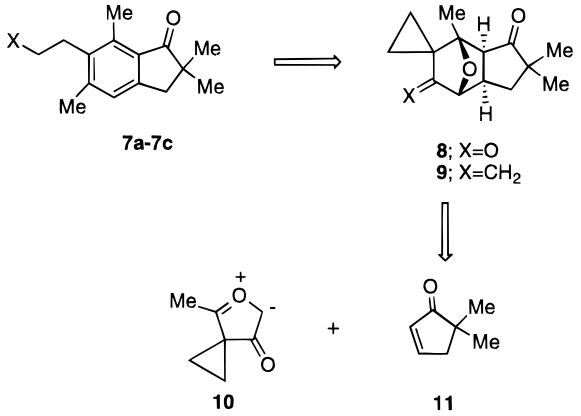
transannular cyclization of the electrophilic carbenoid onto an adjacent carbonyl group to generate a cyclic carbonyl ylide.[14] When an olefin is present, this methodology represents a powerful tool for the construction of polycyclic rings because it creates two new carbon−carbon bonds in a single operation and the reaction allows for high regio- and stereochemical control of the remote substituents.[15] As a consequence of our continuing interest in the development of tandem carbenoid ring-forming reactions in target synthesis,[16] we have applied this approach to the preparation of the pterosin family of sesquiterpenes.

The pterosins (**7**) are a large group of biologically active sesquiterpenes isolated from the bracken fern *Pteridium aquilinium*.[17,18] The carcinogenicity of bracken fern was discovered in 1960 in connection with cattle poisoning[19] which had been reported as early as the 19th century.[20] The major pterosin found in bracken fern is pterosin B (**7**; R = H, X = OH). This compound has been theorized to be formed by decomposition of an unstable precursor, ptaquilosin (**6**), which has also been isolated from bracken.[21] The structures of the pterosins have led to the suggestion[22] that they are derived from farnesyl pyrophosphate (**1**) *via* the same protoilludane precursor **4** which was proposed for the basidiomycete metabolite illudin-M.[23] Evidence for this connection stems from the fact that these natural products are often isolated from the same species[24,25] and that the pterosins can easily be formed by treating ptaquilosin with mild acid.[26] A major obstacle to the synthesis of the pterosins has been the problem of regioselective construction of the penta-substituted aromatic ring. To date, synthetic approaches have relied heavily on classical electrophilic substitution



reactions with their inherent problems of regiocontrol.[27−32] In formulating a strategy for the synthesis of the pterosins, we recognized the potential of the tandem cyclization−cycloaddition reaction of rhodium carbenoids as a method for generating the core skeleton of this class of compounds.[33] On the basis of previous methodological studies,[34] we anticipated that the pterosins could arise from oxabicyclo[2.2.1]octane **8** (X = O). This familiar structure should be easily transformed to the corresponding methylene derivative **9** (X = CH_2) which, in turn, would be expected to undergo an acid-catalyzed rearrangement to the desired target. Cycloadduct **8** should be readily available in a single step by utilizing a bimolecular 1,3-dipolar cycloaddition of carbonyl ylide **10** with cyclopentenone **11**.



Results and Discussion

Our strategy for a short and convergent synthesis of the pterosins has, as its key step, a tandem cyclization−

(14) (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. (b) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.

(15) Padwa, A. In *1,3-Dipolar Cycloaddition Chemistry;* Wiley-Interscience: New York, 1984; Vols. 1 and 2.

(16) (a) Marino, J. P., Jr.; Osterhout, M. H.; Padwa, A. *J. Org. Chem.* **1995**, *60*, 2704. (b) Padwa, A.; Sandanayaka, V. P.; Curtis, E. A. *J. Am. Chem. Soc.* **1994**, *116*, 2667. (c) Curtis, E. A.; Sandanayaka, V. P.; Padwa, A. *Tetrahedron Lett.* **1995**, *36*, 1989.

(17) (a) McMorris, T. C.; Voeller, B. *Phytochemistry* **1971**, *10*, 3253. (b) Yoshishira, K.; Fukuoka, M.; Kuroyanagi, M.; Natori, S. *Chem. Pharm. Bull.* **1971**, *19*, 1491. (c) Bardouille, V.; Mootoo, B. S.; Hirotsu, K.; Clardy, J. *Phytochemistry* **1978**, *17*, 275.

(18) (a) Kobayashi, A.; Egawa, H.; Koshimizu, K.; Mitsui, T. *Agric. Biol. Chem.* **1975**, *39*, 1851. (b) Sengupta, P.; Sen, M.; Niyogi, S. K.; Pakrashi, S. C.; Ali, E. *Phytochemistry* **1976**, *15*, 995. (c) Yoshihira, K.; Fukuoka, M.; Kuroyanagi, M.; Natori, S.; Umeda, M.; Morohoshi, T.; Enomoto, M.; Saito, M. *Chem. Pharm. Bull.* **1978**, *26*, 2346. (d) Yoshihira, K.; Fukuoka, M.; Kuroyanagi, M.; Natori, S. *Chem. Pharm. Bull.* **1979**, *27*, 592.

(19) Evans, I. A. In *Chemical Carcinogens*, 2nd ed.; Searle, C. E., Ed.; American Chemical Society: Washington, DC, 1984; Vol. 2, pp 1171−1204.

(20) Hirono, I.; Yamada, K. In *Naturally Occurring Carcinogens of Plant Origin;* Hirono, I., Ed.; Kodansha-Elsevier: Tokyo Amsterdam, 1987; pp 87−120.

(21) Van der Hoeven, J. C. M.; Lagerweij, W. J.; Posthumus, M. A.; van Veldhuizen, A.; Holterman, H. A. *J. Carcinogenesis* **1983**, *4*, 1587.

(22) McMorris, T. C.; Anchel, M. *J. Am. Chem. Soc.* **1965**, *87*, 1594.

(23) McMorris, T. C.; Kelner, M. J.; Wang, W.; Estes, L. A.; Montoya, M. A.; Taetle, R. *J. Org. Chem.* **1992**, *57*, 6876.

(24) Yoshishira, K.; Kukuoka, M.; Kuroyanagi, M.; Natori, S. *Chem. Pharm. Bull.* **1978**, *26*, 2365.

(25) Ojika, M.; Wakamatsu, K.; Niwa, H.; Yamada, K. *Tetrahedron* **1987**, *43*, 5261.

(26) (a) Niwa, H.; Ojika, M.; Wakamatsu, K.; Yamada, K.; Hirono, I.; Matsushita, K. *Tetrahedron Lett.* **1983**, *24*, 4117. (b) Nozoe, H.; Kobayashi, H.; Urano, S.; Furukawa, J. *Tetrahedron Lett.* **1977**, 1381. (c) Ayer, W. A.; McCaskill, R. H. *Can. J. Chem.* **1981**, *59*, 2150.

(27) Woodward, R. B.; Hoye, T. R. *J. Am. Chem. Soc.* **1977**, *99*, 8007.

(28) Ng, K. M. E.; McMorris, T. C. *Can. J. Chem.* **1984**, *62*, 1945.

(29) Neeson, S. J.; Stevenson, P. J. *Tetrahedron* **1989**, *45*, 6239.

(30) Hayashi, Y.; Nishizawa, M.; Harita, S.; Sakan, T. *Chem. Lett.* **1972**, 375.

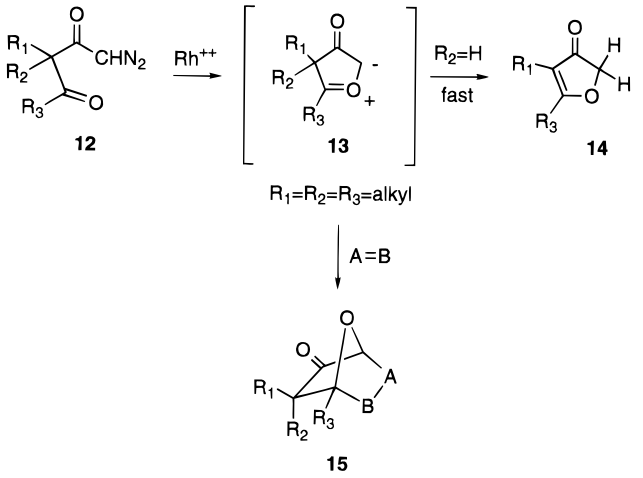
(31) Nambudiry, M. E. N.; Rao, G. S. K. *J. Chem. Soc., Perkin Trans. 1* **1974**, 317.

(32) McMorris, T. C.; Liu, M.; White, R. H. *Lloydia* **1977**, *40*, 221.

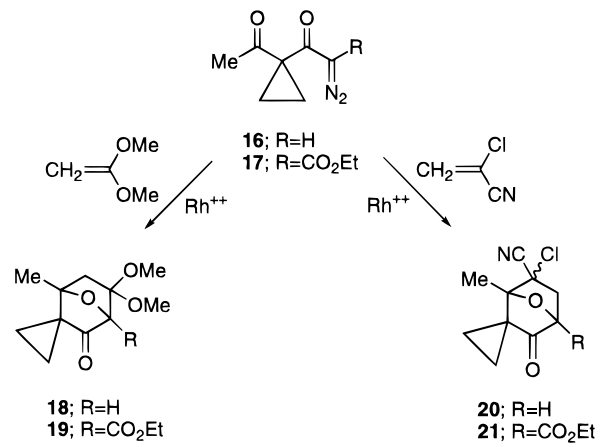
(33) (a) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22. (b) Padwa, A.; Carter, S. P.; Nimmesgern, H. *J. Org. Chem.* **1986**, *51*, 1157.

(34) Padwa, A.; Chinn, R. L. Hornbuckle, S. F.; Zhang, Z. J. *J. Org. Chem.* **1991**, *56*, 3271.

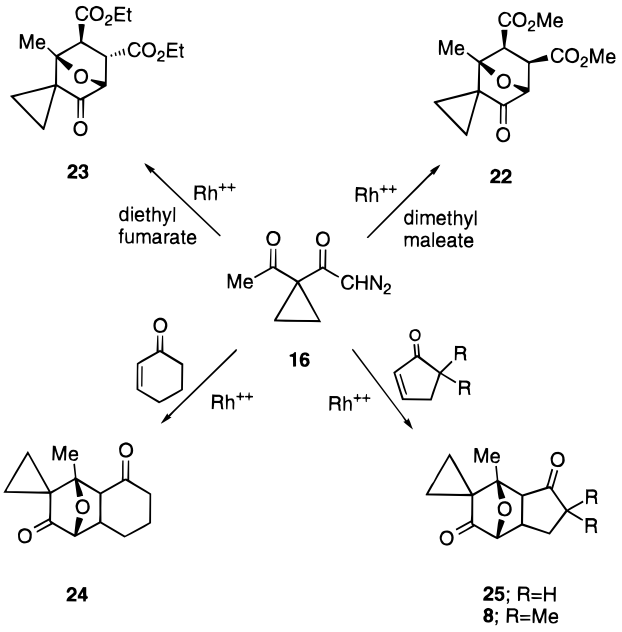
cycloaddition reaction of a rhodium carbenoid.[35−37] In earlier papers we had described the formation of bridged oxabicyclo[3.2.1]octanes from the rhodium(II)-catalyzed reaction of 1-diazopentanediones.[38] Five-membered-ring carbonyl ylides could also be generated by treating 1-diazobutanediones with rhodium(II) carboxylates.[34] However, it was necessary to block the α-position of the 1-diazobutanedione skeleton with two substituent groups in order for the cycloaddition to occur. When only a single substituent group was present, the five-ring dipole was found to transfer a proton at a faster rate than bimolecular dipolar-cycloaddition, leading to furanones of type **14**. The formation of furanone **14** comes as no real surprise since one of the characteristic reactions of carbonyl ylides derived from the reaction of α-diazoalkanes with ketones consists of intramolecular proton transfer.[39−41]



In order to apply the tandem cyclization−cycloaddition sequence to the synthesis of the pterosins, we decided to first establish the viability of the dipolar cycloaddition using the cyclopropanated α-diazo ketones **16** and **17** with a variety of acyclic and cyclic dipolarophiles. The cycloaddition proceeded readily with 1,1-dimethoxyethylene, producing cycloadducts **18** and **19** in 82% yield, respectively. Reaction with 2-chloroacrylonitrile gave the alternate regioisomeric cycloadducts **20** and **21** in 68% and 60% yields as a 3:1 mixture of diastereomers. The assigned regiochemistry follows from the NMR spectra, which show a coupling constant of the bridgehead hydrogen with the adjacent geminal protons of 6.0 and 1.4 Hz with compound **20**. The bridgehead proton corresponds to a singlet with the regioisomeric set of cycloadducts (*i.e.*, **18**). When dimethyl maleate and diethyl fumarate were used as trapping agents, cycloadducts **22** and **23** were obtained as the exclusive products in 76% and 83% yields, respectively. This result provides good support for the concerted nature of the cycloaddition.



Cyclic alkenes also participated in these tandem cyclization−cycloaddition reactions. Among the cyclic alkenones used, the reaction of cyclohexenone with **16** is noteworthy, giving cycloadduct **24** as a 5:1 mixture of diastereomers in 62% yield. A similar reaction occurred with cyclopentenone, producing **25** (74%) as a 4:1 mixture of *exo* and *endo* isomers (see Experimetal Section). The reaction of **16** with 5,5-dimethyl-2-cyclopenten-1-one gave exclusively the *exo* cycloadduct **8** in 80% isolated yield. In all cases, the stereochemical outcome of the cycloaddition favors the *exo* stereoisomer. Apparently the transition state leading to the *endo* isomer suffers from unfavorable steric factors, and consequently the *exo* orientation is favored. The effect of the catalyst on the ratio of products was briefly addressed, but the specific catalyst used *(i.e.* rhodium(II) acetate, rhodium(II) trifluoroacetate, rhodium(II) caprolactamate) did not have a pronounced effect on the distribution of products.

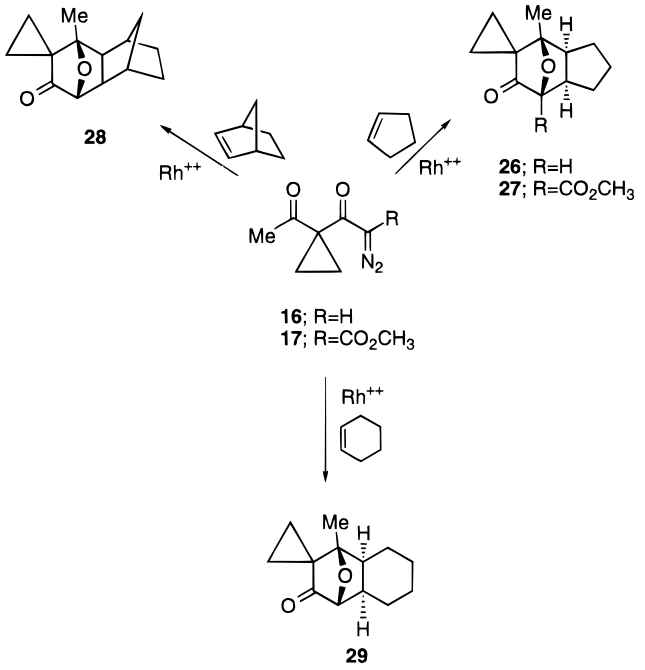


The regioselectivity observed in the above cycloaddition reactions was examined in the light of frontier molecular orbital theory.[42,43] Of the three categories described by Sustmann,[44] type II is particularly common for carbonyl ylides since they possess one of the smallest HOMO−

(35) (a) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (b) Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348.
(36) Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75.
(37) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765.
(38) Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 3100.
(39) (a) Bien, S.; Gillon, A. *Tetrahedron Lett.* **1974**, 3073. (b) Bien, S.; Gillon, A.; Kohen, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 489.
(40) Kharasch, M. S.; Rudy, T.; Nudenberg, W.; Buchi, G. *J. Org. Chem.* **1953**, *18*, 1030.
(41) Lottes, A.; Landgrebe, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, *30*, 4089.
(42) Houk, K. N.; Sims, J.; Duke, R. E.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7287.
(43) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions;* Wiley-Interscience: New York, 1976.

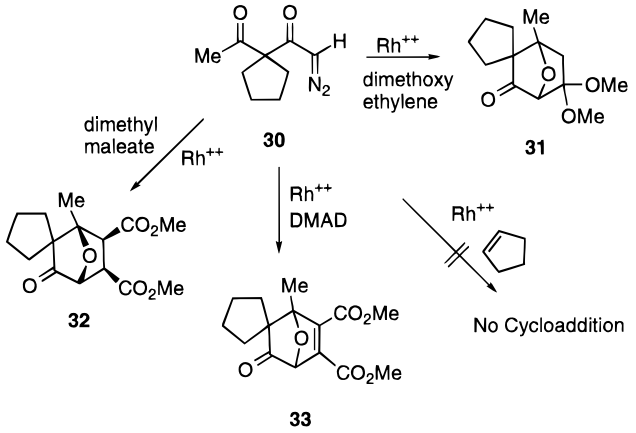
LUMO gaps of the common 1,3-dipoles. According to the FMO treatment of such reactions, the preferred regioisomer will be that in which the atoms bearing larger coefficients of the interacting frontier orbitals overlap. Approximate sizes of the frontier orbital coefficients at the reaction centers of these cyclic carbonyl ylides were calculated by using MOPAC with the PM3 Hamiltonian.[45] The calculations indicate that the atomic coefficient at the α-position (−0.70) is larger than that at the γ-position (+0.56) in the HOMO. The calculations also indicate that the largest coefficient in the LUMO resides on the γ-position (*i.e.*, $\alpha = -0.39$; $\gamma = -0.61$). The HOMO dipole is dominant for reactions with electron deficient dipolarophiles, while the LUMO becomes important for cycloaddition to more electron rich species. Thus, all the regiochemical results outlined above can be readily accommodated in terms of perturbation theory.

We also examined the cycloaddition reaction of α-diazo ketones **16** and **17** with olefins that do not contain electron-withdrawing substituents on the π-bond. To our surprise, the reaction proceeded quite smoothly with cyclopentene (65%) and norbornene (68%). With cyclohexene, cycloadduct **29** was only formed in 16% yield. In



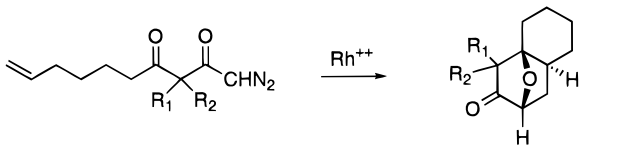
each case the major diastereomer isolated corresponded to the *exo* isomer. The stereochemical assignment follows from the appearance of a singlet for the bridgehead proton. It should be noted that our earlier attempts to induce bimolecular cycloaddition from the reaction of α-diazo pentanediones with unactivated olefins failed.[38] This is presumably related to the large energy gap between the FMOs. We assume that the presence of the spirocyclopropane ring enhances the chemical reactivity of dipole **10** as a consequence of I strain, thereby resulting in an increased reaction rate with the unactivated alkenes.

We next examined the tandem cyclization−cycloaddition reaction using the related five-ring spiro α-diazo ketone **30** since the resulting dipole should possess less I strain. Diazo ketone **30** was efficiently synthesized in four steps from methyl acetoacetate. The first step requires dialkylation with 1,4-diiodobutane, and this was followed by hydrolysis, anhydride formation, and treatment with diazomethane. As expected, **30** undergoes cycloaddition when activated π-bonds were used. Thus, it reacts with 1,1-dimethoxyethylene (60%), dimethyl maleate (36%), and dimethyl acetylenedicarboxylate



(80%), giving rise to the expected cycloadducts **31**−**33**. However, no observable cycloaddition resulted when **30** was treated with $Rh_2(OAc)_4$ in the presence of various unactivated π-bonds. The dipole derived from the cyclopropanated diazo ketone **16** is clearly more reactive toward cycloaddition than the related five-ring spiro system and is probably due to an earlier transition state (*i.e.*, lower activation energy). Another possibility is that the decrease in reaction rate of the dipole derived from the five-ring spiro system **30** is due to a greater degree of steric hindrance in the cycloaddition transition state.

As intramolecular cycloadditions exhibit enhanced reactivity and stereoselectivity over their bimolecular counterparts,[46] we reasoned that the tandem cyclization−cycloaddition reaction of the five-ring spiro system **34** should take place across the unactivated 1-hexenyl π-bond. For comparison purposes, we also examined the comparable cycloaddition reaction using the corresponding spirocyclopropyl system **35** as well as the dimethylated acyclic diazo ketone **36**. The primary spatial



34; R_1, R_2=-$(CH_2)_4$-
35; R_1, R_2=-$(CH_2)_2$-
36; R_1=R_2=Me

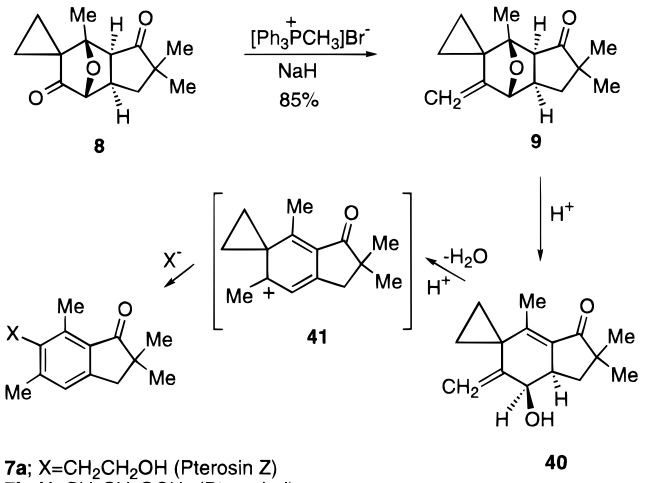
37; R_1, R_2=-$(CH_2)_4$-
38; R_1, R_2=-$(CH_2)_2$-
39; R_1=R_2=Me

requirement for intramolecular cycloaddition of the resulting carbonyl ylide with the neighboring π-bond is that the distance between the two reactive centers be sufficiently close so that effective overlap of the dipole array with the π-bond can occur.[46] Good yields of cycloadducts are generally obtained with tethers leading to six-membered ring formation.[47] Gratifyingly, treatment of **34** with a catalytic quantity of rhodium(II) acetate in CH_2Cl_2 at 25 °C gave the polycyclic adduct **37** in 75% yield

(44) (a) Sustmann, R. *Tetrahedron Lett.* **1983**, *24*, 5425. (b) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 838.
(45) We thank M. D. Weingarten for carrying out these calculations.
(46) Schoffstall, A. M.; Padwa, A. In *Advances in Cycloaddition;* Curran, D. P., Ed.; JAI Press: Greenwich, CT, 1990; Vol. 2, p 1.
(47) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10.

and with complete diastereoselectivity. Intramolecular cycloaddition also occurred using diazo ketones **35** and **36**, producing the related cycloadducts **38** (98%) and **39** (50%). The results encountered with diazo ketone **34** indicate that the rapidity of the intramolecular cycloaddition process significantly overshadows any steric problems in the transition state. Thus, in contrast to the bimolecular situation, the intramolecular cycloaddition reaction of **34** proceeds in comparable efficiency to the three-ring spiro system **36**.

Having established that the dipolar cycloaddition of spirocyclic carbonyl ylides occurred with ease, we next addressed the issue of whether the tandem cyclization−cycloaddition sequence could be used to synthesize several members of the pterosin family of sesquiterpenes. The synthesis began by treating cycloadduct **8** with triphenylmethylphosphonium bromide in the presence of sodium hydride and isolating the expected Wittig product **9** in 85% yield. By using the appropriate acid−solvent combination, we were able to obtain each of the pterosins in one step from the key reactive intermediate **41**. It was



even possible to isolate precursor **40** using either gentle acidic conditions or by treating **9** with *n*-BuLi in THF at 0 °C. Thus, pterosin I[30] (**7b**, X = OCH_3) was formed in quantitative yield by treating **9** with trifluoromethanesulfonic acid in methanol at 25 °C. Pterosin H[31] (**7c**, X = Cl) was obtained in 80% yield from the reaction of **9** with concentrated HCl in DMF, whereas pterosin Z[32] (**7a**, X = OH) was formed (50%) by treating **9** with *p*-toluenesulfonic acid in CH_2Cl_2 followed by an aqueous workup. The overall sequence of reactions can best be described as proceeding by an initial oxy-bridge ring opening followed by dehydration, reprotonation, and a subsequent cyclopropyl carbinyl cation rearrangement.[48] The facility of the process is undoubtedly related to the aromaticity gained in the final step.

In summary, a dipolar cycloaddition strategy has been successfully applied toward the synthesis of several members of the pterosin family of sesquiterpenes. Substrates for the rhodium(II)-catalyzed reaction are readily prepared by the classic alkylation of methyl acetoacetate and conversion to the appropriate α-diazo ketone. The overall transformation represents a highly effective means by which simple starting materials can be converted to the core skeleton of the pterosins in relatively few steps.

(48) (a) Olah, G. A.; Kelly, D. P.; Jeuell, G. L.; Porter, R. D. *J. Am. Chem. Soc.* **1970**, *92*, 2544. (b) Wiberg, K. B.; Szeimies, G. *J. Am. Chem. Soc.* **1970**, *92*, 571. (c) Majerski, Z.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 665.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate−hexane mixture as the eluent unless specified otherwise.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with 1,1-Dimethoxyethylene. A solution containing 70 mg (0.46 mmol) of α-diazo ketone **16**[34] and 0.1 mL (1.0 mmol) of 1,1-dimethoxyethylene in 25 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) octanoate. After stirring at rt for 3 h, the mixture was worked up in the normal fashion to give 80 mg (82%) of 6,6-dimethoxy-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane (**18**) as a white crystalline solid: mp 59−60 °C; IR (CCl_4) 1712, 1446, 1332, 1119, and 1012 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.58−0.62 (m, 1H), 1.02−1.08 (m, 1H), 1.17−1.23 (m, 2H), 1.27 (s, 3H), 1.92 (d, 1H, J = 12.3 Hz), 2.04 (d, 1H, J = 12.3 Hz), 3.26 (s, 3H), 3.28 (s, 3H), and 4.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 13.8, 17.6, 37.2, 46.3, 49.5, 51.1, 84.6, 85.0, 109.8, and 210.0. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.14; H, 7.61.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with 2-Chloroacrylonitrile. A solution containing 116 mg (0.76 mmol) of α-diazo ketone **16** and 80 mg (0.91 mmol) of 2-chloroacrylonitrile in 25 mL of CH_2Cl_2 was treated with a catalytic amount of rhodium(II) octanoate. The reaction was complete after 3 h. The crude oil was purified by silica gel chromatography to give 110 mg (68%) of an inseparable 3:1 mixture of the diastereomers of 7-chloro-7-cyano-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane (**20**): IR (CCl_4) 1759, 1388, and 982 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) major isomer δ 1.13 (m, 1H), 1.30−1.42 (m, 3H), 1.53 (s, 3H), 2.86 (dd, 1H, J = 15 and 1.4 Hz), 2.92 (dd, 1H, J = 15 and 6.0 Hz), and 4.65 (dd, 1H, J = 6.0 and 1.4 Hz); minor isomer δ 1.02 (m, 1H), 1.30−1.42 (m, 3H), 1.57 (s, 3H), 2.40 (d, 1H, J = 15 Hz), 3.27 (dd, 1H, J = 15 and 7 Hz), and 4.60 (d, 1H, J = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 13.7, 14.0, 14.6, 14.8, 15.6, 35.7, 45.4, 46.6, 60.8, 79.6, 79.7, 89.9, 117.3, and 208.1; HRMS calcd for $C_{10}H_{10}NO_2Cl$ 211.0400, found 211.0405.

Preparation of Ethyl 3-(1-Acetylcyclopropyl)-2-diazo-3-oxopropionate (17). To a solution containing 8.9 g (0.05 mol) of 1,1-carbonyldiimidazole in 10 mL of THF was added a solution of 7.0 g (0.05 mol) of 1-acetylcyclopropanecarboxylic acid[34] in 10 mL of THF, and the resulting mixture was stirred at rt for 6 h. To a solution containing 7.2 g (0.05 mol) of 2-carbethoxyacetic acid was added 27 mL (0.1 mol) of isopropylmagnesium bromide at 0 °C. The mixture was stirred for 30 min, warmed to rt, and stirred for an additional 30 min at 40 °C. The magnesium reagent thus prepared was added to the keto acid mixture at −78 °C. The resulting suspension was stirred overnight at rt, the reaction was quenched with water, and the solution was acidified with phosphoric acid to pH 5 and extracted with ether. The product obtained was purified by silica gel chromatography to give 4.5 g (45%) of the expected cyclopropyl keto ester: IR (neat) 1738, 1688, 1360, 1024, and 939 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, 3H, J = 7.2 Hz), 1.51 (m, 2H), 1.60 (m, 2H), 2.06 (s, 3H), 3.69 (s, 2H), and 4.14 (q, 2H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 18.6, 26.0, 42.4, 47.6, 61.1, 148.5, 167.4, 167.5, and 198.8; HRMS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0891.

To a solution containing 0.05 g (2.53 mmol) of the above compound in 10 mL of acetonitrile was added 0.35 mL (2.53 mmol) of triethylamine, and the resulting mixture was stirred for 30 min at rt. A solution containing 306 mg (2.53 mmol) of mesyl azide in 10 mL of acetonitrile was added dropwise over a period of 30 min, and the mixture was stirred for 1 h. The

reaction was quenched with 10% aqueous NaOH solution, and the solution was extracted with CH_2Cl_2. Purification of the product by silica gel chromatography afforded 540 mg (95%) of α-diazoketo ester **17**: IR (neat) 2140, 1735, 1643, 1365, and 1022 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, 3H, J = 7.2 Hz), 1.42 (s, 2H), 1.45 (s, 2H), 2.07 (s, 3H), and 4.23 (q, 2H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 14.3, 16.0, 16.1, 25.4, 42.1, 61.5, 160.8, 187.6, and 202.6.

Rhodium(II)-Catalyzed Reaction of Ethyl 3-(1-Acetylcyclopropyl)-2-diazo-3-oxopropionate (17) with 1,1-Dimethoxyethylene. To a solution containing 300 mg (3.40 mmol) of 1,1-dimethoxyethylene in 10 mL of benzene was added a solution containing 500 mg (2.25 mmol) of α-diazo keto ester **17** in 15 mL of benzene, and the resulting mixture was stirred for 2 h in the presence of 2 mg of rhodium(II) acetate. The product was purified by silica gel chromatography to give 515 mg (81%) of ethyl 6,6-dimethoxy-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane-5-carboxylate (**19**) as a white solid: mp 86−87 °C; IR ($CDCl_3$) 1765, 1726, 1285, 1132, and 1056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (m, 1H), 1.10 (m, 1H), 1.20−1.27 (m, 2H), 1.28−1.33 (m, 6H), 2.00 (d, 1H, J = 12 Hz), 2.26 (d, 1H, J = 12 Hz), 3.24 (s, 3H), 3.37 (s, 3H), and 4.31 (q, 2H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 13.9, 14.3, 17.4, 36.3, 48.2, 49.8, 51.2, 61.8, 81.9, 93.6, 110.5, 163.2, and 202.7. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.21; H, 7.10.

Rhodium(II)-Catalyzed Reaction of Ethyl 3-(1-Acetylcyclopropyl)-2-diazo-3-oxopropionate (17) with 2-Chloroacrylonitrile. To a solution containing 300 mg (3.40 mmol) of 2-chloroacrylonitrile was added a solution containing 500 mg (2.25 mmol) of α-diazo keto ester **17** in 10 mL of benzene in the presence of 2 mg of rhodium(II) acetate. The reaction mixture was stirred for 6 h, and the product was purified by silica gel chromatography to give 383 mg (60%) of an inseparable 3:1 mixture of the diastereoisomers of ethyl 7-chloro-7-cyano-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane-5-carboxylate (**21**): IR (neat) 2137, 1768, 1747, 1260, 1116, and 844 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) major isomer δ 1.05−1.12 (m, 1H), 1.21−1.62 (m, 9H), 3.04 (d, 1H, J = 15 Hz), 3.15 (d, 1H, J = 15 Hz), and 4.32 (q, 2H, J = 7.2 Hz); ^1H NMR (300 MHz, $CDCl_3$) minor isomer δ 0.80−0.90 (m, 1H), 1.21−1.62 (m, 9H), 2.66 (d, 1H, J = 15 Hz), 3.38 (d, 1H, J = 15 Hz), and 4.32 (q, 2H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 13.9, 14.1, 14.6, 15.4, 15.6, 16.4, 35.5, 47.1, 48.3, 62.1, 62.8, 87.2, 88.9, 89.3, 116.6, 163.7, and 203.6; HRMS calcd for $C_{13}H_{14}O_4ClN$ 283.0611, found 283.0607.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with Dimethyl Maleate. To a solution containing 0.5 mL (4.28 mmol) of dimethyl maleate and 2 mg of rhodium(II) acetate in 10 mL of benzene was added 500 mg (3.29 mmol) of a solution of α-diazo ketone **16** in 10 mL of benzene, and the mixture was allowed to stir for 1 h at rt. The reaction mixture was purified by silica gel chromatography to give 670 mg (76%) of dimethyl 4,7-epoxy-4-methyl-8-oxospiro-[2.5]octane-5,6-dicarboxylate (**22**): mp 88−89 °C; IR ($CDCl_3$) 1742, 1429, 1216, 1162, and 987 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75−0.82 (m, 1H), 1.08−1.13 (m, 1H), 1.16−1.20 (m, 1H), 1.23 (s, 3H), 1.29−1.35 (m, 1H), 3.21 (d, 1H, J = 9.6 Hz), 3.34 (d, 1H, J = 9.6 Hz), 3.69 (s, 3H), 3.70 (s, 3H), and 5.03 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 14.4, 14.7, 38.9, 48.3, 52.0, 52.4, 54.3, 81.2, 87.1, 169.5, 170.3, and 210.4. Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.09; H, 6.04.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with Diethyl Fumarate. To a solution containing 340 mg (1.97 mmol) of diethyl fumarate and 2 mg of rhodium(II) acetate in 5 mL of benzene was added a solution containing 200 mg (1.32 mmol) of α-diazo ketone **16** in 5 mL of benzene, and the resulting mixture was allowed to stir for 1 h at rt. The product was purified by silica gel chromatography to give 324 mg (83%) of diethyl 4,7-epoxy-4-methyl-8-oxospiro[2.5]octane-5,6-dicarboxylate (**23**) as a clear oil: IR ($CDCl_3$) 1757, 1729, 1170, and 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81−0.89 (m, 1H), 1.06−1.14 (m, 1H), 1.17−1.36 (m, 2H), 1.22 (s, 3H), 1.20−1.32 (m, 6H), 3.33 (d, 1H, J = 5.3 Hz), 3.88 (dd, 1H, J = 6.2 and 5.3 Hz), 4.07−4.25 (m, 4H), and 4.72 (d, 1H, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.8, 14.0, 14.2, 14.9, 15.1, 39.5, 49.5, 52.8, 61.4, 61.6, 81.6, 88.3, 169.1, 171.3, and 208.9; HRMS calcd for $C_{15}H_{20}O_6$ 296.1260, found 296.1261.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with 2-Cyclopenten-1-one. A solution containing 56 mg (0.37 mmol) of α-diazo ketone **16** and 152 mg (1.9 mmol) of 2-cyclopenenten-1-one in 10 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) octanoate. The reaction was complete after 30 min. The crude residue was purified by silica gel chromatography to give 56 mg (74%) of a 4:1 *exo/endo* mixture of the diastereomers of spiro[1-methyl-10-oxatricyclo[5.2.1.$0^{2,6}$]decane-3,8-dione-9,1′-cyclopropane] (**25**). Recrystallization of the mixture from hexane:ethyl acetate afforded 33 mg (30%) of the *exo* isomer **25a** as a white crystalline solid: mp 128−129 °C; IR (CCl_4) 1758, 1728, 938, and 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.70 (m, 1H), 1.03 (m, 1H), 1.12 (m, 1H), 1.23 (s, 3H), 1.28 (m, 1H), 2.05 (m, 1H), 2.10−2.45 (m, 3H), 2.52 (d, 1H, J = 8.4 Hz), 2.89 (m, 1H), and 4.43 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 13.5, 14.2, 25.3, 38.8, 39.3, 41.4, 57.7, 87.5, 87.9, 211.5, and 216.6. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.72; H, 6.83.

Further crystallization of the mother liquor from hexane: ethyl acetate afforded 22 mg (20%) of the *endo* isomer **25b** as a white crystalline solid: mp 94−95 °C; IR (neat) 1740, 1733, 1453, 1389, and 1160 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (m, 2H), 1.21 (m, 2H), 1.40 (s, 3H), 1.90 (m, 1H), 2.05 (m, 1H), 2.34 (dd, 1H, J = 10.4 and 7.0 Hz), 2.81 (d, 1H, J = 10.4 Hz), 3.44 (m, 1H), and 4.52 (d, 1H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.1, 13.5, 17.1, 18.0, 37.7, 39.4, 44.3, 60.2, 84.8, 86.1, 211.6, and 216.0. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.91; H, 6.85.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with 2-Cyclohexen-1-one. A solution containing 513 mg (3.4 mmol) of α-diazo ketone **16**, and 1.62 g (16.9 mmol) of 2-cyclohexen-1-one in 25 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) octanoate. The reaction was complete after 4 h, giving a 5:1 mixture of disteromeric cycloadducts. The crude oil was purified by silica gel chromatography to afford 451 mg (62%) of spiro[1-methyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undecane-3,9-dione-10,1′-cyclopropane] (**24**) as a white crystalline solid: mp 95−96 °C; IR (CCl_4) 1750, 1687, 1453, 1333, and 993 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.77 (m, 1H), 1.04 (m, 1H), 1.14 (m, 4H), 1.32 (m, 1H), 1.70 (m, 1H), 1.84 (m, 1H), 1.92 (m, 1H), 2.20 (m, 1H), 2.30 (m, 2H), 2.70 (m, 2H), and 4.33 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 14.7, 15.2, 20.1, 27.0, 39.9, 40.3, 40.6, 57.6, 86.2, 88.1, 210.7, and 211.5. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.33. Found: C, 70.92; H, 7.34.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with 5,5-Dimethyl-2-cyclopenten-1-one. A solution containing 2.0 g (15.6 mmol) of 2,2-dimethyl-4-pentenoic acid[49] and 4.2 mL (46.8 mmol) of oxalyl chloride in 25 mL of CH_2Cl_2 was stirred for 3 h at 0 °C. The crude reaction mixture was concentrated under reduced pressure, and the residue was dissolved in 20 mL of CH_2Cl_2. The resulting crude acid chloride solution was added dropwise to a solution containing 4 mL (33.7 mmol) of $SnCl_4$ in 20 mL of CH_2Cl_2 at 0 °C. The reaction mixture was allowed to warm to rt slowly and was stirred for an additional 10 h. The reaction was quenched with ice-cold water, and the solution was extracted with CH_2Cl_2. The organic layer was washed with 1 N HCl, a saturated $NaHCO_3$ solution, and brine. The product was distilled (45 °C, 20 mm) to give 890 mg (53%) of 5,5-dimethyl-2-cyclopenten-1-one:[49] IR (neat) 1742, 1700, 1215, 1123, and 807 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 6H), 2.50 (m, 2H), 6.06 (m, 1H), and 7.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.8, 42.6, 45.5, 131.8, 161.7, and 214.8.

To a solution containing 100 mg (0.91 mmol) of the above enone in 5 mL of benzene was added a solution containing 140 mg (0.91 mmol) of α-diazo ketone **16** in 5 mL of benzene in the presence of 2 mg of rhodium(II) acetate. The reaction mixture was stirred for 4 h at rt, and the product was purified

(49) Creger, P. L. *J. Am. Chem. Soc.* **1967**, *89*, 2500.

to give 110 mg (80%) of the *exo* isomer of spiro[1,4,4-trimethyl-10-oxatricyclo[5.2.1.$0^{2,6}$]decane-3,8-dione-9,1′-cyclopropane] (**8**): mp 120−121 °C; IR ($CDCl_3$) 2958, 1754, 1732, 1381, and 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (m, 1H), 0.93−1.14 (m, 2H), 0.99 (s, 3H), 1.03 (s, 3H), 1.26 (s, 3H), 1.28 (m, 1H), 1.76 (dd, 1H, J = 13.2 and 7.8 Hz), 2.11 (dd, 1H, J = 13.2 and 9.0 Hz), 2.65 (d, 1H, J = 8.4 Hz), 2.82 (q, 1H, J = 8.4 Hz), and 4.23 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8, 13.5, 14.4, 22.5, 25.8, 38.6, 39.5, 40.2, 47.6, 56.2, 85.4, 87.8, 212.3 and 219.3. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.75; H, 7.71.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with Cyclopentene. A solution containing 106 mg (0.70 mmol) of α-diazo ketone **16** and 5 mL (95 mmol) of cyclopentene was treated with 2 mg of rhodium(II) acetate. The reaction was complete after 2 h. The crude oil was purified by silica gel chromatography to give 87 mg (65%) of *exo* spiro[1-methyl-10-oxatricyclo[5.2.1.$0^{2,6}$]decan-8-one-9,1′-cyclopropane] (**26**) as a clear oil: IR (neat) 1752, 1446, 1382, and 991 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (m, 1H), 0.99 (m, 1H), 1.09 (m, 1H), 1.16 (s, 3H), 1.21 (m, 1H), 1.40 (m, 3H), 1.74 (m, 2H), 1.98 (m, 1H), 2.40 (m, 2H), and 4.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.5, 13.6, 13.9, 28.3, 28.8, 31.1, 37.8, 45.4, 51.0, 85.3, 86.1, and 213.8; HRMS calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1150.

Rhodium(II)-Catalyzed Reaction of Ethyl 3-(1-Acetylcyclopropyl)-2-diazo-3-oxopropionate (17) with Cyclopentene. To a solution containing 0.5 mL (5.69 mmol) of cyclopentene and 2 mg of rhodium(II) acetate in 4 mL of benzene was added a solution contaning 150 mg (0.67 mmol) of α-diazo keto ester **17** in 4 mL of benzene, and the resulting mixture was heated at reflux for 5 h. The product was purified by silica gel chromatography to give 126 mg (71%) of *exo* spiro-[7-carbethoxy-1-methyl-10-oxatricyclo[5.2.1.$0^{2,6}$]decan-8-one-9,1′-cyclopropane] (**27**): mp 79−80 °C; IR ($CDCl_3$) 2951, 1761, 1725, 1324, and 1130 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.68−0.75 (m, 1H), 1.02−1.08 (m, 1H), 1.12−1.14 (m, 1H), 1.18 (s, 3H), 1.23−1.48 (m, 4H), 1.30 (t, 3H, J = 7.2 Hz), 1.69−1.80 (m, 2H), 1.95 (m, 1H), 2.43 (q, 1H, J = 8.1 Hz), 2.76 (q, 1H, J = 8.1 Hz), and 4.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.2, 13.8, 14.3, 14.6, 27.9, 28.8, 29.3, 37.7, 48.3, 51.8, 61.6, 85.2, 91.4, 165.8, and 207.2. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.12; H, 7.65.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with Norbornene. To a solution containing 183 mg (2.0 mmol) of norbornene and 2 mg of rhodium(II) acetate in 6 mL of benzene was added a solution contaning 200 mg (1.3 mmol) of α-diazo ketone **16** in 6 mL of benzene, and the resulting mixture was stirred for 6 h at rt. The crude product was purified by silica gel chromatography to give 193 mg (68%) of spiro[5,8-epoxy-1,4-methano-8-methyl-6-oxooctahydronaphthalene-7,1′-cyclopropane] (**28**): mp 67−68 °C; IR ($CDCl_3$) 1747, 1439, 1338, and 1102 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.53−0.62 (m, 1H), 0.82−0.89 (m, 2H), 1.00−1.18 (m, 4H), 1.13 (s, 3H), 1.41 (m, 2H), 1.80 (d, 1H, J = 6.9 Hz), 1.85 (d, 1H, J = 6.9 Hz), 2.11 (d, 1H, J = 9.6 Hz), 2.25 (bs, 1H), 2.31 (bs, 1H), and 4.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.5, 13.3, 13.4, 28.7, 29.2, 34.5, 36.8, 39.8, 40.3, 47.6, 53.5, 84.6, 85.8, and 212.6. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.76; H, 8.29.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (16) with Cyclohexene. A solution containing 97 mg (0.64 mmol) of α-diazo ketone **16** and 5 mL (49.4 mmol) of cyclohexene was treated with 2 mg of rhodium(II) acetate. The reaction was complete in 5 h. The crude oil was purified to give 21 mg (16%) of spiro[1-methyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undecan-9-one-10,1′-cyclopropane] (**29**) as a clear oil: IR (neat) 1752, 1460, 1382, 1332, and 812 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.62 (m, 1H), 0.98 (m, 1H), 1.10 (s, 3H), 1.2−1.7 (m, 10H), 1.90 (m, 1H), 2.10 (m, 1H), and 4.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.6, 13.3, 13.6, 18.1, 18.3, 19.8, 21.8, 38.9, 39.2, 44.1, 85.7, 86.6, and 213.6; HRMS calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1302.

Preparation of 1-Acetyl-1-(diazoacetyl)cyclopentane (30). A solution containing 5.0 g (43 mmol) of methyl acetoacetate, 15.9 g (52 mmol) of 1,4-diiodobutane, and 30 g (215 mmol) of potassium carbonate in 150 mL of DMSO was stirred with a mechanical stirrer at rt overnight. The solution was diluted with 150 mL of H_2O, extracted with ether, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude oil was purified to give 7.27 g (99%) of 1-acetyl-1-carbomethoxycyclopentane[50] as a light yellow oil: IR (neat) 2951, 1740, 1704, 1626, 1432, and 1353 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (m, 4H), 2.10 (m, 4H), 2.17 (s, 3H), and 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 26.3, 32.9, 52.5, 66.7, 173.9, and 203.8; HRMS calcd for $C_9H_{15}O_3$ (M + 1) 171.1021, found 171.1026.

A solution containing 7.0 g (60 mmol) of the above compound and 75 mL of a 3.5 M aqueous KOH solution in 100 mL of MeOH was stirred at rt overnight. The solution was concentrated under reduced pressure and washed with ether, and the aqueous layer was acidified with 50% HCl to pH 2. The acidified solution was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The crude carboxylic acid was not purified, but was immediately used in the next step.

To a solution containing 7.0 g (45 mmol) of the above compound in 150 mL of ether were successively added 5.9 mL (76 mmol) of methyl chloroformate and 8.9 mL (76 mmol) of triethylamine. The solution was stirred under argon at rt for 1 h, and the solid salts were removed by vacuum filtration. This solution was immediately added to a solution containing 100 mmol of diazomethane in ether, and the mixture was stirred at rt overnight. The crude oil was purified by silica gel chromatography to give 4.9 g (50%) of **30** as a yellow oil: IR (neat) 2109, 1713, 1634, 1357, and 1152 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (m, 4H), 2.02 (m, 4H), 2.07 (s, 3H), and 5.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.0, 25.3, 26.0, 31.4, 53.5, 72.5, 192.5, and 204.7; HRMS calcd for $C_9H_{13}N_2O_2$ (M + 1) 181.098, found 181.097.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopentane (30) with 1,1-Dimethoxyethylene. A solution containing 216 mg (1.2 mmol) of α-diazo ketone **30** and 0.40 mL (3.3 mmol) of 1,2-dimethoxyethylene was treated with 2 mg of rhodium(II) acetate. The reaction was complete in 4 h. The crude oil was purified by silica gel chromatography to give 173 mg (60%) of 8,8-dimethoxy-7,10-epoxy-10-methyl-6-oxospiro[4.5]decane (**31**) as a clear oil: IR (neat) 1757, 1456, 1120, and 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (m, 1H), 1.42 (s, 3H), 1.50 (m, 3H), 1.7−1.9 (m, 5H), 2.10 (d, 1H, J = 13.2 Hz), 3.29 (s, 3H), 3.31 (s, 3H), and 4.25 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5, 27.0, 27.1, 33.1, 33.9, 44.2, 49.3, 51.0, 59.7, 84.4, 88.8, 109.3, and 216.2; HRMS calcd for $C_{13}H_{20}O_4$ 240.1361, found 240.1362.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopentane (30) with Dimethyl Maleate. A solution containing 201 mg (1.3 mmol) of α-diazo ketone **30** and 0.4 mL (3.3 mmol) of dimethyl maleate in 5 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) acetate. The reaction was complete after 4 h. The crude oil was purified by silica gel chromatography to give 119 mg (36%) of dimethyl 6,9-epoxy-6-methyl-10-oxospiro[4.5]decane-7,8-dicarboxylate (**32**) as a crystalline solid: mp 113−114 °C; IR ($CDCl_3$) 2954, 1730, 1645, 1439, 1254, and 1005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 3H), 1.44 (m, 1H), 1.52 (m, 2H), 1.76 (m, 4H), 1.99 (m, 1H), 3.03 (d, 1H, J = 9.3 Hz), 3.33 (d, 1H, J = 9.3 Hz), 3.69 (s, 3H), 3.70 (s, 3H), and 4.91 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 26.8, 26.9, 32.2, 33.8, 49.0, 51.9, 52.1, 52.5, 62.2, 81.6, 91.1, 169.6, 170.7, and 217.3. Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.78; H, 6.79.

Rhodium(II)-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopentane (30) with Dimethyl Acetylenedicarboxylate. A solution containing 256 mg (1.4 mmol) of α-diazo ketone **30** and 0.70 mL (5.7 mmol) of DMAD in 5 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) acetate. The reaction was complete after 5 h. The crude residue was purified to give 309 mg (80%) of dimethyl 6,9-epoxy-6-methyl-10-oxospiro[4.5]-dec-7-ene-7,8-dicarboxylate (**33**) as a white crystalline solid: mp 88−89 °C; IR (neat) 1752, 1738, 1720, 1645, 1432, and 1267

(50) (a) Bekhazi, M.; Smith, P. J.; Warkentin, J. *Can. J. Chem.* **1984**, *62*, 1646. (b) Warkentin, J. *J. Org. Chem.* **1984**, *49*. 343.

cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.6−2.0 (s, 3H), 2.60 (m, 8H), 3.80 (s, 3H), 3.85 (s, 3H), and 4.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 26.7, 27.2, 33.6, 33.7, 52.6, 52.7, 52.8, 82.9, 94.0, 138.8, 152.2, 161.3, 163.7, and 211.8. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.12; H, 6.13.

Preparation of Spiro[6,8a-epoxy-7-oxooctahydronaphthalene-8,1′-cyclopentane] (37). To a solution containing 650 mg (5.6 mmol) of methyl acetoacetate in 100 mL THF at 0 °C was added 215 mg (5.6 mmol) of 60% NaH, and the solution was stirred for 30 min. The reaction mixture was cooled to −78 °C, and 3.5 mL (5.6 mmol) of 1.6 M *n*-BuLi in hexane was added. The resulting solution was stirred at −78 °C for 30 min, and then 1.0 g (6.7 mmol) of 5-bromo-1-pentene was added and the solution was allowed to warm to rt over several hours. The mixture was diluted with 100 mL of H_2O, extracted with ether, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification of the crude oil by silica gel chromatography afforded 570 mg (57%) of methyl 3-oxonon-8-ene-1-carboxylate: IR (neat) 1725, 1622, 1430, and 1136 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (m, 2H), 1.61 (m, 2H), 2.05 (dd, 2H, J = 14.2 and 7.2 Hz), 2.54 (t, 2H, J = 7.2 Hz), 3.44 (s, 2H), 3.73 (s, 3H), 4.97 (m, 2H), and 5.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 28.1, 33.3, 42.8, 49.0, 52.2, 114.7, 138.2, 158.0, and 202.5; HRMS calcd for $C_{10}H_{17}O_3$ (M + Li) 185.1178, found 185.1185.

A solution containing 500 mg (2.7 mmol) of the above keto ester, 0.43 mL (3.3 mmol) of 1,4-dibromobutane, and 1.86 g (13.5 mmol) of potassium carbonate in 50 mL of DMSO was stirred at rt overnight. The solution was diluted with 50 mL of water, extracted with ether, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude oil was purified to give 619 mg (100%) of methyl 1-hept-6-enoylcyclopentanecarboxylate as a light yellow oil: IR (neat) 1738, 1709, 1617, and 1431 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (m, 2H), 1.63 (m, 4H), 2.05 (m, 6H), 2.39 (t, 2H, J = 7.3 Hz), 3.18 (m, 2H), 3.67 (s, 3H), 4.97 (m, 2H), and 5.74 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.8, 23.5, 25.6, 28.3, 32.9, 33.5, 33.8, 38.5, 52.4, 66.7, 114.6, 138.4, 174.0, and 205.9; HRMS calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1580.

To a solution containing 407 mg (3.2 mmol) of potassium trimethylsilanolate in 50 mL of ether was added 619 mg (2.7 mmol) of the above ester. The reaction mixture was stirred under argon at rt overnight. The solution was cooled to 0 °C, 1.14 mL (13.5 mmol) of methyl chloroformate was added, and the reaction was allowed to stir for 3 h at rt. The solution was filtered through a fritted funnel and immediately added to 10 mmol of an etheral solution of diazomethane. The solution was allowed to stir overnight, and then the solvent was removed under reduced pressure. The crude oil was purified to give 637 mg (93%) of 1-[1-(2-diazoacetyl)cyclopentyl]-hept-6-en-1-one (**34**) as a yellow oil: IR (neat) 2107, 1702, 1631, and 1339 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (m, 2H), 1.54 (m, 6H), 2.00 (m, 6H), 2.42 (t, 2H, J = 7.2 Hz), 4.92 (m, 2H), 5.18 (s, 1H), and 5.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 25.2, 28.2, 31.7, 33.3, 33.4, 38.4, 53.7, 53.8, 72.8, 114.5, 138.3, 192.8, and 207.4.

A solution containing 20 mg (0.08 mmol) of α-diazo ketone **34** in 5 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) acetate. The reaction was complete after 1 h. The crude oil was purified by silica gel chromatography to give 13 mg (75%) of spiro[6,8a-epoxy-7-oxooctahydronaphthalene-8,1′-cyclopentane] (**37**) as a clear oil: IR (neat) 1752, 1449, and 984 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (m, 2H), 1.4−2.0 (m, 16H), 2.23 (d, 1H, J = 10.4 Hz), and 4.36 (d, 1H, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 25.0, 25.9, 26.6, 26.8, 31.9, 32.0, 33.0, 36.1, 36.6, 61.0, 80.7, 88.5, and 219.9; HRMS calcd for $C_{14}H_{20}O_2$ (M + Li) 227.1627, found 227.1623.

Preparation of Spiro[6,8a-epoxy-7-oxooctahydronaphthalene-8,1′-cyclopropane] (38). A solution containing 80 mg (0.43 mmol) of methyl 3-oxonon-8-ene-1-carboxylate, 0.04 mL (0.52 mmol) of 1,3-dibromoethane, and 290 mg (2.1 mmol) of potassium carbonate in 50 mL of DMSO was stirred at rt overnight. The solution was diluted with 50 mL of water, extracted with ether, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude oil was purified to give 80 mg (93%) of methyl 1-hept-6-enoylcyclopropanecarboxylate as a light yellow oil: IR (neat) 1724, 1618, 1435, and 1138 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (m, 6H), 1.58 (m, 2H), 2.04 (m, 2H), 2.81 (m, 2H), 3.71 (s, 3H), 4.93 (m, 2H), and 5.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 23.6, 28.4, 33.5, 35.0, 41.7, 52.2, 67.5, 114.5, 138.5, 171.5, and 205.0; HRMS calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1252.

A solution containing 1.0 g (4.8 mmol) of the above spiro keto ester and 7.5 mL of 3.5 M KOH in 50 mL of MeOH was stirred at rt overnight. The solution was concentrated under reduced pressure and washed with ether, and the aqueous layer was acidified with 50% HCl to pH 2. The acidified solution was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product obtained was immediately used in the next step.

To a solution containing 859 mg (4.4 mmol) of the above carboxylic acid in 100 mL of ether were successively added 0.41 mL (5.2 mmol) of methyl chloroformate and 0.61 mL (4.4 mmol) of triethylamine. The resulting solution was stirred under argon at rt for 1 h, and the solid salts were removed by vacuum filtration. The solution was immediately added to a solution containing 20 mmol of diazomethane in ether, and the reaction mixture was stirred at rt overnight. The crude oil was purified by silica gel chromatography to give 562 mg (61%) of 1-[1-(2-diazoacetyl)cyclopropyl]hept-6-en-1-one (**35**) as a yellow oil: IR (neat) 2100, 1688, 1624, 1360, 1147, and 912 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.2−1.6 (m, 8H), 2.10 (m, 2H), 2.45 (m, 2H), 4.95 (m, 2H) and 5.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6, 17.7, 23.3, 28.2, 33.4, 39.0, 40.5, 55.7, 114.6, 138.2, 190.3, and 205.6; HRMS calcd for $C_{12}H_{17}N_2O_2$ (M + 1) 221.1290, found 221.1299.

A solution containing 150 mg (0.68 mmol) of α-diazo ketone **35** in 5 mL of CH_2Cl_2 was treated with 2 mg of rhodium(II) acetate. The reaction was complete after 0.5 h. The crude oil was purified by silica gel chromatography to give 125 mg (98%) of spiro[6,8a-epoxy-7-oxooctahydronaphthalene-8,1′-cyclopropane] (**38**) as a clear oil: IR (neat) 1752, 1709, 1440, 1332, and 983 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.65 (m, 1H), 0.9−1.4 (m, 6H), 1.5−2.2 (m, 8H), and 4.50 (d, 1H, J = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.3, 12.3, 21.4, 25.0, 26.7, 32.5, 34.8, 37.3, 39.4, 80.4, 84.2, and 213.6; HRMS calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1146.

Preparation of 10,10-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]-undecan-9-one (39). To a solution containing 0.48 g (19.97 mmol) of NaH in 200 mL of dry THF was added a solution containing 3.5 g (19.02 mmol) of methyl 3-oxonon-8-ene-1-carboxylate, and the reaction mixture was allowed to stir at 0 °C for 30 min. To this mixture was added 1.3 mL (20.9 mmol) of iodomethane in one portion, and the resulting solution was stirred at rt for 15 min. A slurry of 0.48 g (19.97 mmol) of NaH in 25 mL of THF was added, the reaction mixture was stirred for 30 min, and then 1.3 mL (20.9 mmol) of iodomethane was added in one portion. The reaction mixture was stirred for 1 h, the reaction was quenched with a saturated aqueous NH_4Cl solution, and the solution was extracted with ether, washed with brine, and dried over $MgSO_4$. The crude oil was purified by flash silica gel chromatography to give 2.64 g (65%) of methyl 2,2-dimethyl-3-oxonon-8-ene-1-carboxylate as a clear oil: IR (neat) 1739, 1710, and 1456 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.3−1.5 (m, 2H), 1.35 (s, 6H), 1.57 (m, 2H), 2.03 (m, 2H), 2.43 (t, 2H, J = 7.2 Hz), 3.70 (s, 3H), 4.95 (m, 2H), and 5.78 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 23.3, 28.2, 33.5, 37.7, 52.4, 52.5, 55.5, 114.6, 138.4, 174.2, and 207.9.

A solution containing 214 mg (1.0 mmol) of the above compound and 0.86 mL of 3.5 M KOH solution in 50 mL of MeOH was stirred at rt overnight. The mixture was concentrated under reduced pressure and washed with ether, and the aqueous layer was acidified with 50% HCl to pH 2. The acidified solution was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting carboxylic acid was not purified but was used immediately in the next step.

To a solution containing 214 mg (1.0 mmol) of the above acid in 50 mL of ether were successively added 93 μL (1.2 mmol) of methyl chloroformate and 167 μL (1.2 mmol) of NEt_3. The resulting solution was stirred under argon at rt for 1 h,

and the solid salts were removed by vacuum filtration. The solution was immediately added to a solution containing 10 mmol of diazomethane in ether, and the reaction mixture was stirred at rt overnight. The crude oil was purified by silica gel chromatography to give 70 mg (11%) of 1-diazo-3,3-dimethyldec-9-ene-2,4-dione (**36**) as a yellow oil: IR (neat) 2106, 1710, 1632, 1464, and 1340 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 6H), 1.33 (m, 2H), 1.52 (m, 2H), 2.00 (m, 2H), 2.43 (t, 2H, J = 7.2 Hz), 4.97 (m, 2H), 5.31 (s, 1H), and 5.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 23.2, 28.2, 33.4, 38.0, 53.6, 60.1, 114.5, 138.3, 194.1, and 209.1.

A solution containing 70 mg (0.32 mmol) of α-diazo ketone **36** in 5 mL of CH_2Cl_2 was treated with 2 mg of rhodium (II) acetate at rt. The reaction was complete after 1 h. The crude oil was purified by silica gel chromatography to give 30 mg (50%) of 10,10-dimethyl-11-oxatricyclo[6.2.1.$0^{1,6}$]undecan-9-one (**39**) as a clear oil: IR (neat) 1756, 1449, and 985 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.02 (s, 3H), 1.14 (m, 3H), 1.5−1.8 (m, 6H), 2.05 (m, 2H), and 4.36 (d, 1H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 19.9, 21.8, 25.0, 25.7, 32.9, 35.0, 35.5, 50.2, 80.3, 88.2, and 218.1; HRMS calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1316.

Preparation of Spiro[1,4,4-trimethyl-8-methylene-10-oxatricyclo[5.2.1.$0^{2,6}$]decan-3-one-9,1′-cyclopropane] (9). To a solution containing 115 mg (3.0 mmol) of 60% sodium hydride in 20 mL of dry THF was added 1.08 g (3.0 mmol) of triphenylmethylphosphonium bromide, and the resulting mixture was stirred at rt for 1 h. To this mixture was added a solution containing 588 mg (2.5 mmol) of cycloadduct **8** in 5 mL of dry THF, and the reaction mixture was stirred at rt for 5 h. The reaction was filtered through a plug of Celite, diluted with water, extracted with ether, and dried over $MgSO_4$. The product was purified by silica gel chromatography to give 493 mg (85%) of **9** as a white solid: mp 150−151 °C; IR (neat) 1728, 1699, 1451, 1380, and 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.51−0.59 (m, 1H), 0.60−0.65 (m, 1H), 0.67−0.80 (m, 1H), 0.98 (s, 3H), 1.03 (s, 3H), 1.19 (s, 3H), 1.18−1.24 (m, 1H), 1.64 (m, 1H), 2.09 (m, 1H), 2.60−2.68 (m, 2H), 4.22 (s, 1H), 4.55 (s, 1H), and 4.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.3, 13.0, 15.7, 22.5, 26.0, 35.5, 40.7, 43.9, 47.3, 56.6, 85.1, 88.0, 95.9, 156.5, and 221.2. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.54; H, 8.68. Found: C, 77.46; H, 8.62.

Preparation of Spiro[4-hydroxy-2,2,7-trimethyl-5-methylene-2,3,3a,4,5,6-hexahydroinden-1-one-6,1′-cyclopropane] (40). A solution containing 98 mg (0.42 mmol) of **9** and 20 mg (0.12 mmol) of *p*-toluenesulfonic acid in a mixture of 10 mL of methanol and 2 mL of water was stirred at rt for 24 h. The reaction mixture was concentrated under reduced pressure, washed with water, extracted with ether, and dried over $MgSO_4$. Purification of the crude oil by silica gel chromatography afforded 50.8 mg (52%) of spiro[4-hydroxy-2,2,7-trimethyl-5-methylene-2,3,3a,4,5,6-hexahydroinden-1-one-6,1′-cyclopropane] (**40**) as a yellow solid: mp 148−149 °C; IR (neat) 1695, 1645, 1609, and 1453 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.82−0.95 (m, 1H), 1.03 (s, 3H), 1.12 (s, 3H), 1.20−1.29 (m, 1H), 1.30−1.39 (m, 1H), 1.45−1.60 (m, 2H), 1.90 (s, 3H), 2.03−2.05 (m, 1H), 2.19−2.23 (m, 1H), 2.65−2.80 (m, 1H), 4.10 (brs, 1H), 4.63 (s, 1H), and 5.05 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.6, 13.3, 21.4, 24.3, 24.5, 28.4, 41.3, 44.1, 46.3, 75.5, 100.1, 129.7, 150.9, 152.1, and 209.3. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.54; H, 8.68. Found: C, 77.39; H, 8.65.

Preparation of Pterosin Z (7a). A solution containing 25 mg (0.11 mmol) of **9** and 160 mg (0.55 mmol) of *p*-toluenesulfonic acid in 10 mL of CH_2Cl_2 was stirred for 5 h at rt. After aqueous workup, the residue was dissolved in 0.5 mL of dilute HCl (50% v/v) and 10 mL of ethyl acetate and the resulting mixture was heated at reflux for 12 h. The reaction was diluted with water, extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The crude oil was purified by silica gel chromatography to give 13 mg (50%) of pterosin Z (**7a**) as a white solid: mp 87−88 °C (lit.[30] mp 89−90 °C); IR (neat) 1702, 1595, 1460, and 1097 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 6H), 2.44 (s, 3H), 2.70 (s, 3H), 2.87 (s, 2H), 3.20 (t, 2H, J = 8.0 Hz), 3.57 (t, 2H, J = 8.0 Hz), and 7.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.1, 25.5, 31.9, 41.8, 45.6, 61.3, 126.0, 131.2, 134.6, 138.2, 144.0, 151.7, and 212.3.

Preparation of Pterosin I (7b). A solution containing 30 mg (0.13 mmol) of **9** and 0.5 mL of concentrated trifluoromethanesulfonic acid in a mixture of 5 mL of methanol and 2 mL of water was stirred for 1 h at rt. The reaction mixture was concentrated under reduced pressure, washed with water, extracted with ether, and dried over $MgSO_4$. Purification of the crude oil by silica gel chromatography afforded 30 mg (99%) of pterosin I (**7b**) as a white solid: mp 60−61 °C (lit.[31] mp 59−60 °C); IR (neat) 1694, 1596, 1449, and 1379 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 6H), 2.30 (s, 3H), 2.68 (s, 3H), 2.85 (s, 2H), 3.01 (t, 2H, J = 8.0 Hz), 3.38 (s, 3H), 3.45 (t, 2H, J = 8.0 Hz), and 7.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.1, 20.6, 25.0, 28.7, 41.3, 45.0, 58.1, 70.9, 125.3, 130.4, 134.8, 137.6, 143.5, 151.0, and 211.6.

Preparation of Pterosin H (7c). A solution containing 70 mg (0.30 mmol) of **9** and 0.5 mL of concentrated HCl in 5 mL of DMF was stirred at rt for 12 h. The solution was concentrated under reduced pressure, diluted with water, extracted with ether, and dried over $MgSO_4$. The mixture was purified by silica gel chromatography to give 58 mg (80%) of pterosin H (**7c**) as a white solid: mp 87−88 °C (lit.[32] mp 87−88 °C); IR (KBr) 1694, 1596, 1450, and 981 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 6H), 2.43 (s, 3H), 2.68 (s, 3H), 2.86 (s, 2H), 3.18 (t, 2H, J = 8.0 Hz), 3.55 (t, 2H, J = 8.0 Hz), and 7.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.1, 25.5, 32.3, 41.8, 42.1, 45.6, 126.0, 131.2, 134.6, 138.2, 144.0, 151.8, and 212.0.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra for new compounds lacking analyses (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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